REMARKS

Restiction to the Specification under 35 U.S.C. 121:

The Examiner has asked that Applicants restrict the Specification to one of six inventions under §121. Groups I-III describe a compound that can be inserted into a mammal and Groups IV-VI refer to a process of inserting said compound into a mammal. Group I refers to the same compound as Group IV, Group II refers to the same compound as Group V, and Group III refers to the same compound as Group VI. The invention described in the application, constitutes a physiologically labile disulfide bond. A central idea in the invention is the lability of this disulfide bond, i.e., the rate at which the disulfide bond in cleaved in certain conditions. All of the Groups in question concern compounds containing labile disulfide bonds.

Prior art has focused on ways to enhance the stability and slow the cleavage rates of disulfide bonds. In contrast, we describe disulfide bonds that a more labile and have a faster rate of cleavage. This rate is affected by many chemical factors. These factors, while distinct, are intimately interdependent.

For example, for a disulfide bond that is cleaved more rapidly than oxidized glutathione, one of two conditions must be met. Either a constituent thiol of the disulfide bond must have a lower pKa than glutathione or the disulfide bond must be activated by a spatial interaction from a free thiol (an intramolecular attack). Therefore, while a disulfide bond which is cleaved more rapidly than oxidized glutathione does not have to be constructed with a constituent thiol which has a lower pKa than glutathione, as the Office Action correctly states, in order to be labile, that bond must then be activated by intramolecular attack. Similarly, it is also true, as the Office Action states, that a disulfide bond in which one of the constituent thiols has a lower pKa than glutathione is not necessarily cleaved more rapidly than oxidized glutathione. However, for a disulfide bond in which a constituent thiol is defined to have a lower pKa than glutathione, the only other factor to affect the rate of cleavage is the sterics, or spatial interactions, of the system. Steric effects can either promote or inhibit spatial interactions and therefore affect the cleavage of the bond. Thus, in determining the lability and rate of cleavage of a disulfide bond, several

factors are interdcpcndent. In the Applicants' opinion, failure to address these issues concurrently would not allow for effective coverage of the invention presented in the application.

Claim 7 has been amended to obviate the restriction requirement for invention I-III and IV-VI.

The Office action further requests an election of species of transduction signal. It is the Applicants' opinion that the search and examination of all the indicated transduction signals can be made without serious burden. All of the indicated transduction signals are believed to operate by a similar mechanism and publications that specifically study any one of these signals typically makes reference to the others. In addition, all of the transduction signals of claims 2-6 and 8-12 are grouped together and commonly discussed in review articles; see enclosed journal publications. The polynucleotide of claim 13 is not a transduction signal as indicated in the Office Action but a component of the compound of claim 1.

Applicants provisionally elect, with traverse, the group I-III claims if a restriction is still deemed necessary. Within group I-III, Applicants provisionally elect, with traverse, the group I claims if a restriction is still deemed necessary. Applicants also provisionally elect, with traverse, the transduction signal consisting of a polymer containing a cationic charge if a restriction is still deemed necessary.

Respectfully submitted,

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